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Research paper

Self-harm risk between adolescence and midlife in people who experienced separation from one or both parents during childhood

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ABSTRACT

Background: Experience of child-parent separation predicts adverse outcomes in later life. We conducted a detailed epidemiological examination of this complex relationship by modelling an array of separation scenarios and trajectories and subsequent risk of self-harm.

Methods: This cohort study examined persons born in Denmark during 1971–1997. We measured child-parent separations each year from birth to 15th birthday via complete residential address records in the Civil Registration System. Self-harm episodes between 15th birthday and early middle age were ascertained through linkage to psychiatric and general hospital registers. Incidence rate ratios (IRRs) from Poisson regression models were estimated against a reference category of individuals not separated from their parents.

Results: All exposure models examined indicated an association with raised self-harm risk. For example, large elevations in risk were observed in relation to separation from both parents at 15th birthday (IRR 5.50, 95% CI 5.25–5.77), experiencing five or more changes in child-parent separation status (IRR 5.24, CI 4.88–5.63), and having a shorter duration of familial cohesion during upbringing. There was no significant evidence for varying strength of association according to child's gender.

Limitations: Measuring child-parent separation according to differential residential addresses took no account of the reason for or circumstances of these separations.

Conclusions: These novel findings suggest that self-harm prevention initiatives should be tailored toward exposed persons who remain psychologically distressed into adulthood. These high-risk subgroups include individuals with little experience of familial cohesion during their upbringing, those with the most complicated trajectories who lived through multiple child-parent separation transitions, and those separated from both parents during early adolescence.

1. Introduction

The American Psychological Association has highlighted that more than 9 out of 10 people in Western cultures marry by age 50 years, and that healthy marriages promote wellbeing for children and help to protect them from mental, physical, educational and psychosocial difficulties. However, the Association also reported that around 40–50% of first marriages in the United States end in divorce, with the divorce rate for subsequent marriages being higher still (http://www.apa.org/topics/divorce/index.aspx). The majority of children whose parents divorce or separate grow up to be well-functioning adults (Hetherington, 1993; Afifi et al., 2009). However, previous research has demonstrated that exposure to this common phenomenon during childhood is linked with elevated suicidality risk in later years; specifically, attempted suicide and suicidal ideation in the US national population (Afifi et al., 2009), in Montreal, Canada (Tousignant et al., 1993) and in Scania, southern Sweden (Lindström and Rosvall, 2015); attempted suicide in the US national population (Lizardi et al., 2009; Alonzo et al., 2014); suicidal ideation in the Canadian national population (Fuller-Thomson and Dalton, 2011); and death by suicide in New York City, USA (Gould et al., 1998).

Most children living in developed countries more frequently experience separation from one or both parents than parental death during upbringing, but this exposure may be more strongly linked with the development of psychopathology than the impact of parental loss (Canetti et al., 2000). Despite the existence of a sizeable body of

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literature on this topic, strong and consistent evidence is lacking concerning variability in degree of heightened self-harm risk according to which parent the child was separated from, the age at which separation occurred, child's gender, the duration of separation from one or both parents, and the total number of separations and subsequent reunions during a child's upbringing. For example, there are conflicting reports as to which gender has the greater elevation in suicidality risk (Lizardi et al., 2009; Fuller-Thomson and Dalton, 2011).

To better understand the pathways that link these exposures with elevated self-harm risk, we examined interlinked national Danish administrative registers. This large cohort study provided total population coverage and abundant statistical power for modelling the various scenarios and trajectories of child-parent separation and later risk of self-harm. These data sources enabled us to examine all separations from one or both parents according to complete and accurate residential address information for the whole national population. They also provided us with a rare opportunity to examine adverse outcomes over the longer term (Chase-Lansdale et al., 1995; Jónsson et al., 2000; Huurre et al., 2006) well into adult maturity, although the registry data did not enable us to examine self-harm cases with and without suicidal intent separately. Our goal was to generate novel evidence concerning varying approaches to examining exposure to child-parent separation and its association with later self-harm risk, to inform future interventions and preventive initiatives.

2. Methods

2.1. Study population

This investigation was approved by the Danish Data Protection Agency. The study population consisted of persons born in Denmark from 1st January 1971 to 31st December 1997. The cohort was delineated using the Danish Civil Registration System (CRS) (Pedersen et al., 2006), which has provided continuously updated computerised data on the whole population since 1968. The CRS routinely captures demographic information, including gender, date of birth, identity of parents and siblings and vital status, on all Danish residents. We restricted the cohort to individuals born in Denmark and living there on their 15th birthday, with both parents also born in Denmark and alive on the cohort member's 15th birthday.

2.2. Self-harm classification

Cohort members were linked via their unique personal identifiers to the Danish Psychiatric Central Research Register (Mors et al., 2011), which has recorded all psychiatric admissions since 1969, and to the National Patient Register (Lynge et al., 2011), which has captured all general hospital admissions since 1977. Both registers have also recorded all outpatient episodes, including emergency room visits, from 1995 and onwards. Diagnoses were made by treating clinicians and assigned according to the Danish modification of the International Classification of Diseases (ICD); 8th revision prior to 1994 (WHO, 1967) and 10th revision from 1994 onwards (WHO, 1992). Self-harm was defined by ICD diagnosis and/or 'self-harm' or 'attempted suicide' being the recorded reason for hospital contact. We examined follow-up time from 15th birthday to the first subsequent registered self-harm episode. For a more detailed description of the self-harm classification used in this investigation, please see Nordentoft et al., 2011.

2.3. Child-parent separation exposure classifications

Our measure of child-parent separation was based on complete recording of all periods in which a child did not live with one or both parent/s. Residential addresses have been recorded in the CRS since 1971, and Danish residents are legally required to notify the authorities of any change to their permanent address. Child-parent separation was based on cohort members residing or not residing with their legal parent/s, and was measured at birth and at each birthday from 1st to 15th, inclusive. Separation status was defined as: no separation (living with both parents); paternal separation (living with the mother, but not father); maternal separation (living with father, but not mother); maternal and paternal separation (living with neither parent); or missing (unknown), as in an earlier study by Paksarian et al. (2015). Persons separated from both parents at birth and who subsequently lived with at least one parent prior to their 15th birthday, along with individuals with missing child-parent separation status information for at least one year, were excluded; i.e. 1.4% of the initial cohort. Children who resided abroad at one of their birthdays prior to their 15th birthday, who accounted for 1.3% of the cohort studied, were included and were assumed to be living with their parent/s if they also lived abroad in the same country.

We examined child-parent separation between birth and 15th birthday using seven different exposure models, and we compared these against each other to better understand the complex association between child-parent separation and elevated self-harm risk. The classifications we examined were as follows:

1) Child-parent separation status at birth
2) Child-parent separation status at 15th birthday
3) Age at first child-parent separation
4) Duration of child-parent separation
5) Duration of familial cohesion
6) Total number of changes in child-parent separation status
7) Array of specific child-parent separation trajectories

A change in separation status was defined as when a cohort member shifted from experiencing one kind of separation status one year to another in the subsequent year, which might occur just once, multiple times, or never. For classification 7, 'Array of specific child-parent separation trajectories', all change sequences were included if the whole trajectory accounted for at least 0.1% of the total population examined.

2.4. Study design and analysis

Persons were followed from their 15th birthday until their first registered self-harm episode, emigration from Denmark, death or the end of the study (31st December 2012), whichever came first. Persons with a registered self-harm episode prior to their 15th birthday were excluded. Incidence rate ratios (IRRs) for self-harm were estimated from Poisson regression models (Laird and Olivier, 1981) along with likelihood ratio-based 95% confidence intervals (CIs) and likelihood ratio tests, using the GENMOD procedure of SAS 9.4. Age and calendar year were treated as time-dependent variables, and all IRRs reported were adjusted for calendar year, age, gender, and interactions between these variables, whilst also accounting for changes in gender and age-specific incidence by calendar year, to produce non-significant score tests for overdispersion (Breslow, 1996). We fitted additional models adjusted for parental socioeconomic status during the year that cohort members reached their 15th birthdays, according to the following measures: 1. Income in annual quintiles; 2. Highest educational level attained (primary school, high school/vocational training, higher education); 3. Employment status (employed, unemployed, outside workforce for other reasons).

The Akaike Information Criterion (AIC) (Akaike, 1974) considers a model's goodness-of-fit in relation to the number of parameters used to fit the model. For the seven different exposure classification models examined, the one with the smallest AIC value was designated as having the optimal fit to the data; i.e. the exposure classification that best describes the association between child-parent separation and elevated self-harm risk. This approach allows for comparison between

Table 1
Incidence rate ratios for self-harm from age 15 according to child-parent separation status at birth, at 15th birthday, and by number of changes in separation status through upbringing.

Child-parent separation status	Exposure prevalence (%)	*n* persons (self-harm)	Incidence rate[a]	IRR[b]	(95% CI)	Adj. IRR[c]	(95% CI)
Separation status at birth:							
Not separated	93.4	26,601	17.5	1.00	(Ref.)	1.00	(Ref.)
Separated from father	6.2	3747	36.1	2.12	(2.05–2.20)	1.53	(1.48–1.58)
Separated from mother	0.17	66	16.7	1.28	(1.00–1.62)	1.16	(0.90–1.46)
Separated from both parents	0.21	70	12.0	1.07	(0.84–1.35)	0.94	(0.73–1.17)
Separation status at 15th birthday:							
Not separated	71.2	15,734	13.1	1.00	(Ref.)	1.00	(Ref.)
Separated from father	22.8	10,660	31.3	2.23	(2.17–2.28)	1.83	(1.79–1.88)
Separated from mother	4.2	2084	32.8	2.44	(2.33–2.55)	2.02	(1.93–2.12)
Separated from both parents	1.7	2006	66.2	5.50	(5.25–5.77)	3.30	(3.14–3.46)
No. of separation status changes:							
0	67.7	14,644	12.9	1.00	(Ref.)	1.00	(Ref.)
1	21.1	8696	26.7	1.99	(1.94–2.04)	1.72	(1.68–1.77)
2	6.3	3459	36.1	2.68	(2.58–2.78)	2.17	(2.09–2.25)
3	3.1	2039	42.8	3.16	(3.01–3.31)	2.30	(2.19–2.41)
4	1.0	856	54.4	4.02	(3.75–4.30)	2.67	(2.49–2.86)
5 or more	0.7	790	71.9	5.24	(4.88–5.63)	3.17	(2.94–3.41)

[a] Incidence rate per 10,000 person-years at risk.
[b] IRR - Incidence rate ratio.
[c] Adj. IRR - Adjusted incidence rate ratio; adjusted for parental socioeconomic status at cohort members' 15th birthdays.

models that are not nested (i.e. most exposure-outcome models examined in this study), which is not possible with likelihood ratio methods. As a sensitivity analysis we also calculated the Bayesian (or 'Schwarz') Information Criterion (BIC) (Schwarz, 1978).

3. Results

3.1. Child-parent separation status at birth and at 15th birthday

The study cohort consisted of 1,343,129 persons born in Denmark during 1971–1997 who were followed up from their 15th birthdays. In this cohort 30,484 individuals harmed themselves during 16.3 million person-years at risk, 1986–2012: a crude incidence rate of 1.87 per 1000 person-years. The great majority (93.4%) of cohort members lived with both parents at their birth (Table 1). Compared to these persons, those who were separated from their father at birth had a more than doubled risk of self-harm beyond their 15th birthday. Individuals separated from their mothers at birth had a modestly elevated risk, and for those separated from both parents at birth there was no evidence of an association in either direction. At 15th birthday, 71.2% of cohort members lived with both their parents and a further 22.8% lived only with their mother (Table 1). Those separated from their mother or their father had a more than doubled risk, and children separated from both parents had the largest risk elevation (5–6 times higher) compared to those living with both parents on their 15th birthday. Table 1 also shows IRRs additionally adjusted for parental socioeconomic status in the year that cohort members reached their 15th birthdays. Although these confounding variables accounted for a sizeable proportion of the elevated risks observed, essentially the same patterns of risk persisted across the various child-parent exposure models examined.

3.2. Total number of changes in child-parent separation status during upbringing

Between their births and 15th birthdays, 67.7% of cohort members were not exposed to any changes in child-parent separation status, and the more separation status changes experienced during childhood the greater the elevation in later risk of self-harm (Table 1). Statistical interaction terms indicated no significant evidence of differential associations by offspring gender in relation to child-parent separation at birth (P=0.20) and at 15th birthday (P=0.14), and by total number of changes in separation status during upbringing (P=0.75). Table 1 also shows IRRs adjusted for parental socioeconomic status. The association was attenuated somewhat with this additional adjustment, but a risk gradient remained nonetheless.

3.3. Age at first child-parent separation

Compared to cohort members not exposed to child-parent separation, those who experienced separation had elevated risk of subsequent self-harm, irrespective as to whether they were separated from their mother, father or both parents and also the age at which they first experienced child-parent separation (Fig. 1). The association was generally stronger for paternal than for maternal separation, and especially so if separation from father first occurred during infancy or early childhood. If first separation occurred between 10th and 15th birthday there was little evidence of a difference in strength of association for separation from father versus mother. The association with age at first maternal separation was quite stable across yearly ages of exposure. Individuals first-separated from both parents before 10th birthday had elevated risk of later self-harm, with IRR values for age-year at separation ranging from between 1.4 and 2.2. For those persons exposed to first separation from both parents between 10th and 15th birthday we observed a steep gradient of rising risk with increasing age at first separation.

3.4. Duration of familial cohesion and of child-parent separation during upbringing

Incidence rate ratios for duration of familial cohesion during upbringing are plotted in Fig. 2, against a reference category of 15 complete years of living with both parents. This shows a clear trend toward rising risk the shorter the duration of cohesion, although a steep gradient was only observed for less than five years of familial cohesion. For periods of familial cohesion of more than five years duration the IRR values were more modest although they were still significantly elevated compared with the full 15 years of cohesion reference category. Fig. 3 presents IRR estimates for duration of child-parent separation in years against a reference category of zero years of separation between birth and 15th birthday. The strength of association with duration of paternal separation was slightly stronger than it

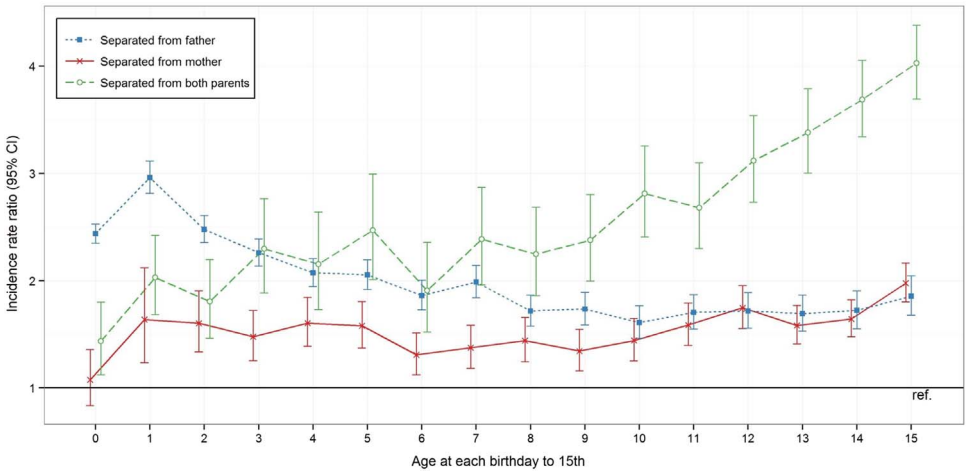

Fig. 1. : Incidence rate ratios for self-harm from age 15 according to age at first child-parent separation event during upbringing. Footnote: Each incidence rate ratio presented had its own reference category, which consisted of individuals who did not experience the particular type of child-parent separation (separated from mother / father / both parents) at any age during their upbringing.

was for maternal separation, and for both of these exposures the strength of association increased gradually the longer the duration of separation. With duration of separation from both parents, a quite different pattern was observed. Being separated from both parents for 1–12 years conferred far higher risk of later self-harm than being separated from mother or father only for the equivalent length of time in the 1–12 years range; by contrast, being separated from both parents for 14 or 15 years was linked with lower risk than separation for this length of time from mother or father only.

3.5. Specific child-parent separation trajectories

Incidence rate ratios for specific child-parent separation trajectories, versus a reference group of cohort members who were never separated from either parent between birth and 15th birthday, are presented in Table 2. The trajectories with the highest incidence rates and IRRs for subsequent self-harm were:

1) *Separated from father only at birth → separated from both parents ('F→FM')*: IRR 7.25, 95% CI 6.42–8.14 (adjusted for parental SES: IRR 3.89, 3.44–4.38)
2) *Living with both parents at birth → separated from father only → separated from both parents ('N→F→FM')*: IRR 6.92, 6.33–7.54 (adjusted for parental SES: IRR 4.08, 3.73–4.46)
3) *Living with both parents at birth → separated from father only → separated from both parents → separated from father only ('N→F→FM→F')*: IRR 6.04, 5.22–6.94 (adjusted for parental SES: IRR 3.84, 3.31–4.41).

For each of these three high-risk subgroups, a common experience was transition from being separated from one's father only to being separated from both parents. Another striking finding that Table 2 reveals is the consistency of the link between child-parent separation and later elevated risk of self-harm. Thus, risk was raised even for the six subgroups of cohort members who were reunited with both parents at the same residential address on reaching their 15th birthday. These are the trajectory subgroups that have the letter 'N' (i.e. separated from neither parent) as their final separation status transition in the table.

3.6. Goodness-of-fit comparison across multiple exposure models: AIC values

For each of the seven specific child-parent separation classifications modelled we calculated the Akaike Information Criterion (AIC), as presented in Table 3. The exposure classification with the closest fit to the data, and that therefore best described the association, was age at first child-parent separation. Duration of separation and of familial cohesion also yielded especially good fits. The highest AIC value

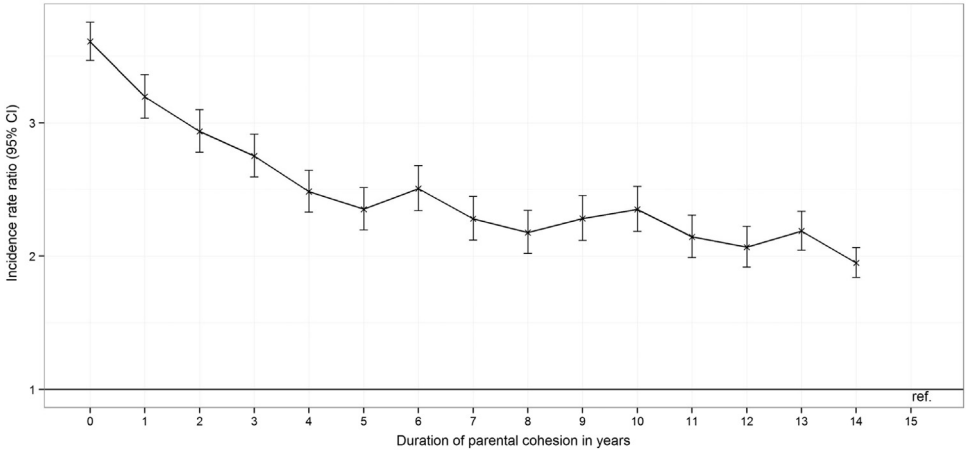

Fig. 2. : Incidence rate ratios for self-harm from age 15 according to duration in years of familial cohesion between birth and 15th birthday. Footnote: No incidence rate ratio value is presented for 15 years on the X-axis because this was the reference category (i.e. IRR =1.0; the child experienced no period of separation from either or both of their parents between their birth and their 15th birthday).

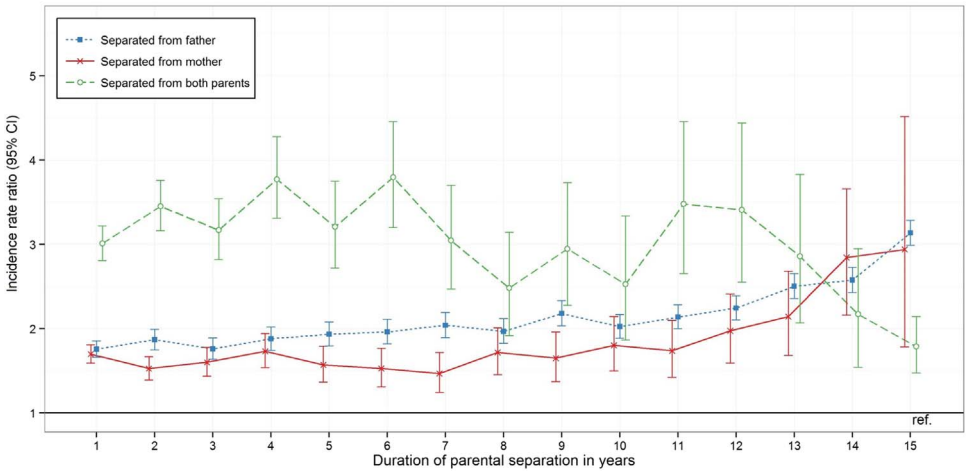

Fig. 3. : Incidence rate ratios for self-harm from age 15 according to duration in years of child-parent separation between birth and 15th birthday. Footnote: The reference category was constant for each of the 15 time-point measurements during upbringing; it consisted of individuals who experienced 15 complete years of not being separated from their mother, their father or either parent, depending on the specific type of child-parent separation under consideration.

observed was in relation to child-parent separation status at birth, indicating the poorest fit for the seven exposure models examined. The rank order of the AIC values did not change with additional adjustment of the models for parental socioeconomic status during the year that cohort members reached their 15th birthdays. As a sensitivity analysis, we also calculated Bayesian Information Criterion (BIC) values, and the same rank order according to goodness-of-fit was observed across the various exposure classifications as for the AIC values reported in Table 3 (results not shown).

4. Discussion

4.1. Main findings

Our population-based cohort study has generated unique evidence illustrating how relative risk of self-harm in the longer term up to early middle age varies across various exposure classifications reflecting child-parent separation during upbringing. Self-harm risk was consistently elevated for each exposure model in the set that we examined. The consistency and strength of association observed indicates that child-parent separation may be an important component in the aetiology of self-harm in the general population. The exposure classifications age at first separation, duration of separation, and duration of familial cohesion produced the best model fits. Especially large risks elevations were observed for being separated from both parents during early adolescence and at 15th birthday, passing through a greater number of separation status transitions, and experiencing a shorter duration of familial cohesion during upbringing. Child-parent separation was consistently linked with elevated self-harm risk, even for those subgroups where cohort members were reunited with both parents by

Table 2
Incidence rate ratios for self-harm from age 15 in relation to specific child-parent separation trajectories during upbringing with an exposure prevalence of 0.1% or greater.

Separation trajectories[a]	Exposure prevalence (%)	*n* persons (self-harm)	Incidence rate[b]	IRR[c]	(95% CI)
N	65.5	13,350	12.1	1.00 (ref.)	–
N→F	16.3	6518	27.1	2.07	(2.01–2.14)
N→F→N	2.5	968	25.6	1.97	(1.84–2.10)
N→M	2.2	809	23.1	1.94	(1.81–2.08)
F	2.0	1222	39.2	3.10	(2.93–3.29)
F→N	1.9	701	19.2	1.72	(1.59–1.85)
N→F→N→F	1.6	880	35.4	2.72	(2.53–2.91)
N→F→M	1.1	643	44.4	3.28	(3.03–3.55)
F→N→F	0.91	531	36.8	3.01	(2.75–3.27)
N→M→F	0.55	244	32.0	2.41	(2.12–2.73)
N→F→FM	0.40	522	86.5	6.92	(6.33–7.54)
N→FM	0.39	309	43.3	4.03	(3.59–4.50)
N→M→N	0.33	107	19.7	1.62	(1.33–1.94)
N→F→M→F	0.29	208	58.1	4.02	(3.49–4.60)
N→F→N→F→N	0.28	170	39.9	3.01	(2.58–3.49)
FM	0.21	70	12.0	1.48	(1.16–1.86)
F→FM	0.21	278	92.6	7.25	(6.42–8.14)
F→N→F→N	0.21	108	30.6	2.49	(2.05–2.99)
N→F→N→F→N→F	0.17	131	49.6	3.77	(3.15–4.45)
N→F→FM→F	0.16	192	69.3	6.04	(5.22–6.94)
N→FM→N	0.15	105	34.7	3.34	(2.74–4.03)
F→N→F→N→F	0.14	96	41.7	3.35	(2.72–4.07)
N→F→N→M	0.14	82	38.2	3.05	(2.44–3.77)
N→F→N→F→M	0.12	87	53.3	3.91	(3.14–4.79)
All other trajectories	2.3	2153	58.4	4.86	(4.64–5.09)

[a] N = Separated from neither parent; F = separated from father; M = separated from mother; FM = separated from both parents.
[b] Incidence rate per 10,000 person-years at risk.
[c] IRR - Incidence rate ratio.

Table 3
Akaike Information Criterion (AIC) values indicating goodness-of-fit for each exposure model examined.

Child-parent separation trajectories	Rank[a]	AIC	Additional d.f.[b]
Child-parent separation status at birth	7	138014	3
Child-parent separation status at 15th birthday	5	132557	3
Age at first child-parent separation	1	130273	48
Duration of child-parent separation in years	2	130374	45
Duration of familial cohesion in years	4	132238	15
Total no. of changes in child-parent separation status	6	132922	5
Array of specific child-parent separation trajectories	3	130740	24

[a] The AIC values are ranked smallest to largest; the smaller the AIC value, the better the model fit.
[b] The AIC value for the 'initial' model fit included only the adjustment variables (with 232 degrees of freedom, d.f.) and did not include a child-parent separation exposure variable. This column indicates the additional degrees of freedom in the model according to each of the seven exposure variables added separately.

their 15th birthday. Parental socioeconomic status in the year that cohort members reached their 15th birthdays attenuated the observed associations to some degree, although the patterns of risk across the multiple exposure categories examined remained essentially unchanged. There was no significant evidence for varying strength of association according to offspring gender in relation to child-parent separation.

4.2. Comparison with existing evidence

The findings generated by this study cannot be compared directly with existing research evidence, because no previously published studies have examined this association according to this array of different child-parent separation scenarios and trajectories. Previous studies of this topic have examined offspring gender differences, but there is a lack of consistent evidence for variability in strength of association between male and female offspring (Lindström and Rosvall, 2015). Thus, some authors have reported higher risk of suicidality in males exposed to parental divorce or child-parent separation (Donald et al., 2006; Fuller-Thomson and Dalton, 2011), whereas others have reported greater risk in females (Huurre et al., 2006; Lizardi et al., 2009). Our study was therefore unusual in finding no evidence for clear gender differences in the strength or direction of the observed associations. A further inconsistency in the existing literature concerns effect size variability according to age at which divorce or child-parent separation occurred. A large cross-sectional study from Sweden with a 52% response rate reported highest odds ratios for suicidal thoughts in individuals who experienced exposure at age 0–4 years (Lindström and Rosvall, 2015), whereas an analysis of the longitudinal 1958 National Child Development Study (NCDS) from Great Britain reported evidence that divorce at 11–16 years potentially had the most deleterious impact on subsequent mental health in young adults (Chase-Lansdale et al., 1995). Our findings concur with the small body of previous literature reporting that children exposed to multiple child-parent separation transitions tend to experience the worst outcomes (Capaldi and Patterson, 1991), and that the strength of association is larger in relation to separation from both parents as opposed to just one (Canetti et al., 2000). These particular family types are likely to have the greatest number of serious and intractable psychosocial difficulties.

4.3. Interpretation

These findings and those generated from other studies of parental divorce and child-parent separation should be interpreted with caution, and causal relationships cannot be assumed and should not be inferred. It is possible, however, that the separation events in themselves traumatise children and adolescents who experience them. Acute shock and disruption, along with an ongoing sense of loss of family togetherness, could lead directly to later psychological distress, mental illness and self-harming behaviour. On the other hand, the observed associations may be explained by familial genetic or environmental determinants that predispose parents to dysfunctional and ultimately failed relationships and also their offspring to psychopathology in later life (Cherlin et al., 1998; Huurre et al., 2006). In some particularly troubled families, where children are exposed to parental substance misuse, domestic violence or inter-parental conflict, parental divorce or separation may actually be beneficial to them (Hetherington and Stanley-Hagan, 1999; Alonzo et al., 2014).

In Fig. 1 we observed a gradient of increasing risk with rising age beyond age 11 with separation from both parents, although no such gradient was observed in relation to separation from either father or mother. The risk gradient linked with separation from both parents during early adolescence may merely reflect closeness in time between exposure and outcome. However, whilst remaining cautious about making causal inferences from our observations, a speculative potential alternative explanation is that separation from both parents during early adolescence is a particularly harmful to the wellbeing of these young people, at a crucial time in their development as they move toward making the transition from childhood to adulthood. Another possible interpretation is that separation from both parents at this age is likely to entail residential relocation, which we have previously reported as being strongly linked with elevated risk for these two adverse outcomes (Webb et al., 2016).

Our study found no evidence of elevated risk among those individuals who were registered as having a different residential address to both of their legal parents at birth. This may indicate that Danish social services agencies are effectively looking after those infants who are transferred into their care from the very start of their lives.

4.4. Strengths and limitations

This cohort study was conducted in the entire Danish population using prospectively collected registry data that were unbiased owing to knowledge of subsequent self-harm episodes. Danish healthcare is provided to all citizens free of charge at the point of access, which precluded ascertainment bias in identifying hospital-presenting self-harm episodes. The Civil Registration System provided a unique national resource for measuring changes in residential address and thereby child-parent separation transitions in the whole population for each age-year from birth up to 15th birthday. We had abundant statistical power and precision to assess all of the exposure-outcome relationships examined. Our measurement of child-parent separation was based entirely on residential address information. Thus, it was free of recall or social desirability biases in the course of later self-reporting of childhood adversity (Susser and Widom, 2012), which is a widely acknowledged major limitation of most published studies on this topic (Aro, 1988; Afifi et al., 2009; Lizardi et al., 2009; Fuller-Thomson et al. 2011; Alonzo et al., 2014; Lindström and Rosvall, 2015). Those studies that relied on subject self-reporting were also mostly cross-sectional in design, which limited the degree to which aetiological inferences could be drawn. Our investigation thus belongs to a small set of more robust cohort studies with long-term follow-up (Allison and Furtsenberg, 1989; Chase-Lansdale et al., 1995; Rodgers et al., 1997; Cherlin et al., 1998; Gilman et al., 2003). By classifying self-harm according to ICD coding and other information captured by general hospital and psychiatric hospital registers, we used a stringent case ascertainment procedure that may have 'missed' a sizeable proportion of self-harm occurrences in the population. We believe this is preferable to using a

less stringent classification that would inadvertently pick up numerous false positive cases. Thus, although some of the incidence rate ratios we reported are large, they are nonetheless conservative estimates of relative risk (Copeland et al., 1977).

However, our study did have some important limitations. First and foremost, we had no information regarding the reason for and contextual circumstances of the changes in child-parent separation status. Second, the aggregated estimates generated will have masked heterogeneity of association, an issue that is common to many population-level epidemiological studies. Thus, we could not discern nested subgroups of individuals who were resilient to the apparent negative impact of child-parent separation, and those who may have benefitted from being separated from an abusive or substance-dependent parent (Hetherington and Stanley-Hagan, 1999; Wolchik et al., 2009; Alonzo et al., 2014). Third, we cannot exclude the possibility that problematic behaviours in children could be the main precipitant of child-parent separation. This effect, which we had no means of assessing in the registry data, would have inflated the observed relative risk estimates due to reverse causality bias (Maselko et al., 2012). Specifically, this type of bias may partly explain the markedly elevated risk of self-harm linked with separation from both parents during early adolescence.

Fourth, we did not adjust for confounding by parental mental illness. Attempting to account for these problems prior to separation would likely have been problematic using the national registry data. Many of the mental health problems that are precursors to familial fragmentation, including common conditions like stress, anxiety, depression and alcohol misuse (Kessler et al., 1998), would not result in secondary care treatment episodes and so they would not be identified in the Psychiatric Central Research Register. The more severe episodes are captured in this register, but many antecedent mental health problems would only be identified as having an onset after the separation event, with many of these parents presenting to services only after their marriage or partner relationship had broken down. Finally, with the registry data that were available to us we could not separately identify episodes of self-harm with and without suicidal intent. We examined self-harm using a previously developed classification according to persons registered as having been admitted for treatment in a general hospital or a psychiatric unit following a self-harm episode. We can, however, be confident that the classification identified a larger proportion of genuine suicide attempts and a smaller proportion of non-suicidal self-injury cases than one would expect to observe in a sample of all cases of self-harm that occur in the general population.

4.5. Implications and conclusions

This national cohort study adds weight to existing published evidence indicating that a troubled upbringing, as indicated by separation from one or both parents, may be linked with harmful long-term mental health problems through late adolescence, young adulthood and on to early middle age. The U.S. National Institutes of Health-funded 'New Beginnings Program' (https://asupreventionresearch.com/) has been shown to be effective in ameliorating the potentially harmful impact of child-parent separation and divorce across multiple outcome domains (Wolchik et al., 2009 , 2013; Sigal et al., 2012; Herman et al., 2015). The novel findings generated from our cohort study suggest that future interventions could be tailored toward subgroups of exposed individuals who are psychologically distressed into adulthood, including those separated from both of their parents and particularly during early adolescence, those with little experience of familial cohesion throughout their upbringing, and those with the most complex trajectories who lived through many transitions of child-parent separation. Future research could usefully compare outcomes among younger or older unexposed siblings who did not experience child-parent separation. This approach would account for unmeasured genetic and familial environmental confounders and thereby enable stronger inferences to be drawn regarding potential for causality. On the basis of the findings we have reported, preventive efforts should not focus specifically on one gender over the other in meeting the complex needs of people with psychological problems who experienced separation from one or both parents whilst growing up.

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